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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/552,206	09/14/2006	Irina Velikyan	PH0333	6320
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PRINCETON, NJ 08540-6231				
EXAMINER				
PERREIRA, MELISSA JEAN				
ART UNIT		PAPER NUMBER		
1618				
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03/23/2010		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

10/552,206

**Applicant(s)**

VELIKYAN ET AL.

**Examiner**

MELISSA PERREIRA

**Art Unit**

1618

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 14 January 2010.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-19 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-19 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/C)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_
- Paper No(s)/Mail Date \_\_\_\_\_

### DETAILED ACTION

Claims 1-19 are pending in the application.

#### ***Double Patenting***

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. The rejection of claims 1,2 and 6-14 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of copending Application No. 10/552,134 is maintained as no terminal disclaimer was filed.

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The rejection of claims 1,2 and 6-14 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 and 7-13 of copending Application No. 11/358,681 is maintained as no terminal disclaimer was filed.

### ***New Grounds of Rejection Necessitated by the Amendment to the Claims***

#### ***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Griffiths et al. (WO03/059397A2) in view of Bottcher et al. (US 5,439,863) and further in view of Maier-Borst et al. (GB 2056471A) and Wheaton et al. (*Industrial and Engineering Chemistry* **1951**, 43, 1088-1093).

6. Griffiths et al. (WO03/059397A2) discloses the method of obtaining the  $^{68}\text{Ga}$  and the method of producing a  $^{68}\text{Ga}$ -radiolabeled complex/ $^{68}\text{Ga}$ -labeled targeting agent for use in PET detection (p4, paragraph 2; p9, paragraph 1). The method of obtaining the  $^{68}\text{Ga}$  involves eluting  $^{68}\text{Ga}$  from a  $^{68}\text{Ge}/^{68}\text{Ga}$  titanium dioxide based in-house generator. The  $^{68}\text{Ga}$  is eluted from the titanium dioxide generator with acidic solution, such as 0.5-1N HCl (p7, paragraph 3; p8, paragraph 2; p12, paragraph 1). The  $^{68}\text{Ge}/^{68}\text{Ga}$  may be optionally fitted with an anion-exchange membrane/Q5F cartridge (p14, paragraph 1). The method of producing a radiolabeled gallium complex involves reacting the solution of a peptide labeled macrocyclic chelate with the  $^{68}\text{Ga}$  diluted from the  $^{68}\text{Ge}/^{68}\text{Ga}$  titanium dioxide generator (p14, paragraph 1). The chelate-targeting agent conjugates can be compounded into kits that are ready to use and accept the  $^{68}\text{Ga}$  elute (p8, paragraph 3). The macrocyclic-chelating agent, such as DOTA or NOTA may be linked to a peptide that can target the site of a disease, thus generating a bifunctional chelating agent comprising a targeting vector which will be site-specific (p9, paragraph 1; p11, paragraphs 1 and 2).
7. Griffiths et al. does not disclose the preparation of the chelate-targeting agent conjugates via microwave acceleration. Griffiths et al. also does not disclose an anion exchanger comprising  $\text{HCO}_3^-$  or more specifically one comprising an amine functional groups or one based on polystyrene-divinylbenzene.
8. Bottcher et al. (US 5,439,863) discloses the preparation of metal complex salts via microwave irradiation (column 3, line 44-46). The complexes are prepared from metal ions and multitoothed chelating ligands that occupy more than one coordination

site on the central metal atom (column 3, lines 55-59; column 4, lines 44-46). The ligands of the disclosure may include those with dioxime (N and O containing), etc. groups (column 5, lines 20-24). The use of microwave as the high-energy input allows for a continuous conversion, single-stage reaction with short reaction time and ease of separation of the formed complexes (column 4, line 19; column 5, lines 66+; column 6, lines 1-5).

9. Maier-Borst et al. (GB 2056471A) discloses the separation of  $^{68}\text{Ga}$  from its parent nuclide,  $^{68}\text{Ge}$ . The elution of a  $^{68}\text{Ge}/^{68}\text{Ga}$  generator with 5N, 0.5N HCl and water is followed by a.) contacting the eluant from the generator column with an anion exchanger comprising quaternary ammonium groups incorporated in a matrix of styrene and divinylbenzene and b.) subsequent washing of the anion exchanger with water (p4, lines 44-48). The anion exchanger of the disclosure encompasses the anion exchanger of the instant claims and therefore is capable of the same functions, such as binding  $^{68}\text{Ga}$  and has the same properties. Further, the wash water of the disclosure is capable of eluting the bound  $^{68}\text{Ga}$  from the anion exchanger as evidenced by the specification p9, example 1.

10. Wheaton et al. (*Industrial and Engineering Chemistry* **1951**, 43, 1088-1093) discloses strongly basic anion exchange resins which are quaternary ammonium salts having a polystyrene crosslinked with divinylbenzene base (Dowex 1 and 2) (p1088, paragraph 1). Dowex 1 and 2 are provided in various ionic forms, such as bicarbonate (table I; table II). The bicarbonate form of the dowex 2 is shown to have increased

stability for several days, even at higher temperatures (p1088, chemical stability, third paragraph; p1089, figure 3).

11. At the time of the invention it would have been obvious to produce a  $^{68}\text{Ga}$ -DOTA-peptide complex for use as a PET tracer via the production of  $^{68}\text{Ga}$  from a  $^{68}\text{Ge}/^{68}\text{Ga}$  titanium dioxide generator as disclosed by Griffiths et al. The microwave synthesis technique for the method of producing metal-chelate complexes was known by Bottcher et al. thus, it would have been obvious to utilize the microwave acceleration technique for a faster, more reproducible preparation of the  $^{68}\text{Ga}$ -DOTA-peptide complex, such as that of Griffiths et al. to generate a complex useful in the treatment or diagnosis of tumours with minimal side product formation. Microwave acceleration techniques have been utilized since the 1980's in a number of production methods for radioactive precursors and radiotracers labeled with positron-emitting nuclides. The microwave method is mostly associated with shortened reaction times and encompasses the microwave conditions of the instant claims. Since the microwave technique was known in the art (Bottcher et al.) one would have a reasonable expectation of success for preparing radiotracer via labeling reactions with this improved microwave technique.

12. It is known in the prior art to add a chelating agent, such as EDTA to elute  $^{68}\text{Ga}$  from an aluminum oxide exchanger. The disadvantage of forming the  $^{68}\text{Ga}$ -EDTA complex is that the complex has to be destroyed before further processing to obtain radiopharmaceutical agents which is time-consuming and expensive (see Maier-Borst et al. p1, lines 10-16). It would have been obvious to one ordinarily skilled in the art to utilize the anion exchanger of Maier-Borst et al. to separate  $^{68}\text{Ga}$  from its parent nuclide

since no chelating agent is required for separation, as Maier-Borst et al. is drawn to the same method of the separation of  $^{68}\text{Ga}$  from  $^{68}\text{Ge}$  without the use of an EDTA chelating agent. Thus, it would have been predictable and favorable to utilize the anion exchanger of Maier-Borst et al. to avoid the extra step of destroying a  $^{68}\text{Ga}$ -EDTA for further processing to obtain radiopharmaceutical agents.

13. At the time of the invention it would have been obvious to one ordinarily skilled in the art that the anion exchange resin comprising quaternary ammonium groups incorporated in a matrix of styrene and divinylbenzene may comprise the bicarbonate counterion as the bicarbonate provides for increased stability for days, even at higher temperatures, and minimal amount of swelling and thus greater selectivity of the anion exchange resin (Wheaton et al. p1089, resin swelling).

14. Claims 1,3-7 and 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Maier-Borst et al. (GB 2056471A) in view of Wheaton et al. (*Industrial and Engineering Chemistry* 1951, 43, 1088-1093).

15. Maier-Borst et al. (GB 2056471A) discloses the separation of  $^{68}\text{Ga}$  from its parent nuclide,  $^{68}\text{Ge}$ . The elution of a  $^{68}\text{Ge}/^{68}\text{Ga}$  generator with 5N, 0.5N HCl and water is followed by a.) contacting the eluant from the generator column with an anion exchanger comprising quaternary ammonium groups incorporated in a matrix of styrene and divinylbenzene and subsequent washing of the anion exchanger with water (p4, lines 44-48). The anion exchanger of the disclosure encompasses the anion exchanger of the instant claims and therefore is capable of the same functions, such as binding



$^{68}\text{Ga}$  and has the same properties. Further, the wash water of the disclosure is capable of eluting the bound  $^{68}\text{Ga}$  from the anion exchanger as evidenced by the specification p9, example 1.

16. Maier-Borst et al. does not disclose the anion exchanger comprising  $\text{HCO}_3^-$  as counterions.

17. Wheaton et al. (*Industrial and Engineering Chemistry* **1951**, 43, 1088-1093) discloses strongly basic anion exchange resins which are quaternary ammonium salts having a polystyrene crosslinked with divinylbenzene base (Dowex 1 and 2) (p1088, paragraph 1). Dowex 1 and 2 are provided in various ionic forms, such as bicarbonate (table I; table II). The bicarbonate form of the dowex 2 is shown to have increased stability for several days, even at higher temperatures (p1088, chemical stability, third paragraph; p1089, figure 3).

18. At the time of the invention it would have been obvious to one ordinarily skilled in the art that the anion exchange resin comprising quaternary ammonium groups incorporated in a matrix of styrene and divinylbenzene may comprise the bicarbonate counterion as the bicarbonate form provides for increased stability for days, even at higher temperatures, and minimal amount of swelling and thus greater selectivity of the anion exchange resin.

19. At the time of the invention it would have been obvious to one ordinarily skilled in the art to assemble the necessary components used for the method of obtaining  $^{68}\text{Ga}$ , such as columns, etc. into a kit for the

***Response to Arguments***

20. Applicant's arguments filed 1/14/10 have been fully considered but they are not persuasive.
21. Applicant asserts that Wheaton et al. teaches that there are 5 resins (iodide, bromide, nitrate, nitrite and chloride) that would all have superior characteristics to bicarbonate with regards to the minimizing the swelling characteristics of the resin.
22. Wheaton et al. teaches that the bicarbonate form of the dowex 2 is shown to have increased stability for several days, even at higher temperatures and minimal swelling (4%) wherein the anion form of the dowex with the maximum swelling is 13%. The bicarbonate form of the dowex 2 is one of a finite number of anionic forms of the dowex 2. Therefore, it would have been obvious to one skilled in the art to utilize an anion resin form which is stable over several days for multiple use of the resin material.
23. Applicant asserts that Maier-Borst et al. refers to an aluminum oxide column for the  $^{68}\text{Ga}$  generator which is completely different than titanium oxide of the instant claims.
24. Maier-Borst et al. was not used to teach of a titanium oxide generator column.
25. Griffiths et al. was used to teach of the method of obtaining the  $^{68}\text{Ga}$  via a  $^{68}\text{Ge}/^{68}\text{Ga}$  titanium dioxide based in-house generator which may be optionally fitted with an anion-exchange membrane.
26. Maier-Borst et al. was used to teaches of contacting the eluant from a  $^{68}\text{Ge}/^{68}\text{Ga}$  generator column with an anion exchanger comprising quaternary ammonium groups incorporated in a matrix of styrene and divinylbenzene and subsequent washing of the

anion exchanger with water. The anion exchanger of the disclosure encompasses the anion exchanger of the instant claims and therefore is capable of the same functions, such as binding  $^{68}\text{Ga}$  and has the same properties. Further, the wash water of the disclosure is capable of eluting the bound  $^{68}\text{Ga}$  from the anion exchanger as evidenced by the specification p9, example 1.

27. Therefore, it would have been obvious to one skilled in the art to contact the elute from a  $^{68}\text{Ge}/^{68}\text{Ga}$  generator column, such as that of Griffiths et al. with an anion exchanger, such as that of Maier-Borst et al. to separate  $^{68}\text{Ga}$  from its parent nuclide,  $^{68}\text{Ge}$  since no chelating agent is required for separation, as Maier-Borst et al. is drawn to the same method of the separation of  $^{68}\text{Ga}$  from  $^{68}\text{Ge}$  without the use of an EDTA chelating agent. Thus, it would have been predictable and favorable to utilize the anion exchanger of Maier-Borst et al. to avoid the extra step of destroying a  $^{68}\text{Ga}$ -EDTA for further processing to obtain radiopharmaceutical agents.

### ***Conclusion***

No claims are allowed at this time.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MELISSA PERREIRA whose telephone number is (571)272-1354. The examiner can normally be reached on 9am-5pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/

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Supervisory Patent Examiner, Art Unit 1618

/Melissa Perreira/

Examiner, Art Unit 1618